US-PAT-NO: 6248516
DOCUMENT-IDENTIFIER: US 6248516 B1
TITLE: Single domain ligands, receptors comprising said ligands methods for their
production, and use of said ligands and receptors
DATE-ISSUED: June 19, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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Ward; Elizabeth Sally	Cambridge	N/A	N/A	GBX
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US-CL-CURRENT: 435/6,435/252.33 ,435/441 ,435/446 ,435/69.6

CLAIMS:

What is claimed is:
1. A library for expression of immunoglobulin heavy chain variable domains (VH
domains), said library comprising a repertoire of nucleic acid sequences encoding a
third CDR of an immunoglobulin heavy chain variable domain, each member of said
repertoire being flanked by VH sequences so as to provide nucleic acid encoding a
repertoire of immunoglobulin heavy chain variable domains which are identical except
for said third CDR.
2. A library according to claim 1 wherein said third CDRs are derived from
preexisting repertoires of CDRs.
3. A library according to claim 1 wherein said third CDRs comprise random
sequences.
4. A library according to claim 1 wherein said nucleic acid encoding a repertoire
of immunoglobulin heavy chain variable domains further comprises a sequence encoding
one or more constant domains for expression of Ig-type chains.
5. A method for generating an antibody variable domain expression library having a
diversity of CDR3 sequences, said method comprising:
providing expression vectors, said vectors comprising a variable domain encoding
sequence of an antibody;
introducing by mutagenesis a diversity of CDR3 sequences into

said variable domain
encoding sequence; and
recovering an expression library having a diversity of binding activities.
6. The method of claim 5 wherein said antibody variable domain is a VH domain.
7. The method of claim 5 wherein said expression vector encodes an Fab antibody
fragment.
8. The method of claim 5 wherein said expression vector encodes a scFv fragment.
9. An expression library which expresses antibody variable domains, said library
comprising a universal set of framework regions carrying a diversity of CDR3
sequences, said library having a diversity of binding activities.
10. The expression library of claim 9 wherein said antibody variable domains are VH
domains.
11. The expression library of claim 9 wherein said antibody variable domains are VL
domains.
12. The expression library of claim 9 wherein said variable domains are expressed
in the form of Fab antibody fragments.
13. An expression library which expresses antibody variable domains having CDR
diversity in only the CDR3 sequences, said library having a diversity of binding
activities.
14. The expression library of claim 13 wherein said antibody variable domains are
VH domains.
15. The expression library of claim 13 wherein said antibody variable domains are
VL domains.
16. The expression library of claim 13 wherein said variable domains are expressed
in the form of Fab antibody fragments.
17. The expression library of claim 13 wherein said variable domains are expressed
in the form of scFv antibody fragments.
18. An expression library produced by the method of claim 5.
19. An expression library produced by the method of claim 6.
20. An expression library produced by the method of claim 7.
21. An expression library produced by the method of claim 8.

US-PAT-NO: 6225447
DOCUMENT-IDENTIFIER: US 6225447 B1
TITLE: Methods for producing members of specific binding pairs
DATE-ISSUED: May 1, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Winter; Gregory Paul	Cambridge	N/A	N/A	GBX
Johnson; Kevin Stuart	Cambridge	N/A	N/A	GBX
Griffiths; Andrew David	Cambridge	N/A	N/A	GBX
Smith; Andrew John	Cambridge	N/A	N/A	GBX

Hammond
US-CL-CURRENT: 530/387.3

CLAIMS:

What is claimed is:
1. A specific binding pair member which is a single chain specific binding pair member comprising a first polypeptide chain component and a second polypeptide chain component and specific for a complementary specific binding pair member of interest, produced by a method which comprises:
(I) introducing into host cells;
(i) first vectors comprising nucleic acid encoding a genetically diverse population of a first polypeptide chain component fused to a component of a secreted replicable genetic display package for display of said polypeptide chain component at the surface of replicable genetic display packages; and
(ii) second vectors comprising nucleic acid encoding a genetically diverse population of said second polypeptide chain component;
said first vectors being packaged in infectious replicable genetic display packages and their introduction into host cells being by infection into host cells harboring said second vectors; or
said second vectors being packaged in infectious replicable genetic display packages and their introducing into host cells being by infection into host cells harboring said first vectors;

(II) causing or allowing recombination between said first and second vectors within
said host cells, the recombination being promoted by inclusion in said first and
second vectors of sequences at which site-specific recombination occurs resulting in
recombinant vectors each of which comprises nucleic acid encoding a said single
chain specific binding pair member comprising a said first polypeptide chain
component and a said second polypeptide chain component and an amino acid sequence
encoded by a sequence provided by recombination between said sequences at which
site-specific recombination occurs, and capable of being packaged into a replicable
genetic display packages using said replicable genetic display package component;
(III) expressing said single chain specific binding pair members within the host
cells to form a library of said single chain specific binding pair members displayed
by replicable genetic display packages, whereby the genetic materials of each said
replicable genetic display package encodes a single chain specific binding pair
member displayed at its surface,
(IV) selecting by binding with said complementary specific binding pair member of
interest one or more single chain specific binding pair members specific for said
complementary specific binding pair member of interest, each single chain specific
binding pair member thus selected being associated in its respective replicable
genetic display package with nucleic acid encoding that single chain specific
binding pair member,
(V) obtaining nucleic acid encoding a said single chain specific binding pair member
from its replicable genetic display package displaying a single chain specific
binding pair member selected in step (IV);
(V) producing, by expression of encoding nucleic acid in a recombinant host
organism, a single chain specific binding pair member comprising a first polypeptide
chain component and a second polypeptide chain component and an amino acid sequence
encoded by a sequence provided by recombination between said sequences at which

site-specific recombination occurs and specific for said complementary specific
binding pair member of interest, which single chain specific binding pair comprises
a polypeptide chain component which is as encoded by nucleic acid encoding a said
polypeptide chain component of a specific binding pair member selected in step (IV)
or is a derivative thereof by way of addition, deletion, substitution or insertion
of one or more amino acids or by linkage of another molecule.
2. A specific binding pair member according to claim 1 wherein at least one of said
first and second vectors is a phage vector.
3. A specific binding pair member according to claim 1 wherein expression in said
step (III) is from a phagemid vector, the method including using a helper phage or a
plasmid expressing complementing phage genes, to help package said phagemid genome,
and said component of the replicable genetic display package is a capsid protein
therefor.
4. A specific binding pair member according to claim 1 wherein either or both of
the populations of said first and second polypeptide chain components is derived
from a repertoire selected from the group consisting of:
(i) the repertoire of rearranged immunoglobulin genes of an animal immunized with a
complementary sbp member;
(ii) the repertoire of rearranged immunoglobulin genes of an animal not immunized
with a complementary sbp member;
(iii) a repertoire of an artificially rearranged immunoglobulin gene or genes;
(iv) a repertoire of an immunoglobulin homolog gene or genes;
(v) a repertoire of sequences derived from a germ-line immunoglobulin gene or genes;
(vi) a repertoire of an immunoglobulin gene or genes artificially mutated by the
introduction of one or more point mutations; and
(vii) a mixture of any of (i), (ii), (iii), (iv), (v) and (vi).
5. A specific binding pair member according to claim 1 wherein the replicable
genetic display package is a bacteriophage, the host is a bacterium, and said
component of the replicable genetic display package is a capsid protein for the
bacteriophage.
6. A specific binding pair member according to claim 5 wherein

the phage is a
filamentous phage.
7. A specific binding pair member according to claim 6 wherein the phage is
selected from the class I phages fd, M13, If1, Ike, ZJ/Z, Ff and the class II phages
Xf, Pf1 and Pf3.
8. A specific binding pair member according to claim 6 wherein the first
polypeptide chain components are expressed as fusions with the gene III capsid
protein of phage fd or its counterpart in another filamentous phage.
9. A specific binding pair member according to claim 8 wherein the first
polypeptide chain components are each inserted in the N-terminal region of the
mature capsid protein downstream of a secretory leader peptide.
10. A specific binding pair member according to claim 5 wherein the first
polypeptide chain components are expressed as fusions with the gene III capsid
protein of phage fd or its counterpart in another filamentous phage.
11. A specific binding pair member according to claim 10 wherein the first
polypeptide chain components are each inserted in the N-terminal region of the
mature capsid protein downstream of a secretory leader peptide.
12. A specific binding pair member according to claim 5 wherein the host is E.
coli.
13. A specific binding pair member according to claim 1, wherein said sequences at
which site-specific recombination occurs are loxP sequences.
14. A specific binding pair (sbp) member which is a single chain specific binding
pair member specific for a counterpart specific binding pair member of interest,
produced by a method which comprises:
(i) causing or allowing intracellular recombination between (a) first vectors
comprising nucleic acid encoding a population of a fusion of a first polypeptide
chain component of a specific binding pair member and a component of a secreted
replicable genetic display package and (b) second vectors comprising nucleic acid
encoding a population of a second polypeptide chain component of a specific binding
pair member, at least one of said populations being genetically

diverse, the
recombination between the vectors being at sequences at which site-specific
recombination occurs and resulting in recombinant vectors each of which comprises
nucleic acid encoding a single chain specific binding pair member comprising a said
first polypeptide chain component, a said second polypeptide chain component, and an
amino acid sequence encoded by a sequence provided by recombination between said
sequences at which site-specific recombination occurs, which nucleic acid is capable
of being packaged using said replicable genetic display package component; and
(ii) expressing said single chain specific binding pair members producing replicable
genetic display packages which display at their surface said single chain specific
binding pair members and which each comprise nucleic acid encoding a said single
chain specific binding pair member
(iii) selecting by binding with said counterpart specific binding pair member of
interest one or more single chain specific binding pair members specific for said
counterpart specific binding pair member of interest, each single chain specific
binding pair member thus selected being associated in its respective replicable
genetic display package with nucleic acid encoding that single chain specific
binding pair member;
(iv) obtaining nucleic acid encoding a said single chain specific binding pair
member from its replicable genetic display package displaying a specific binding
pair member selected in step (v);
(v) producing, by expression of encoding nucleic acid in a recombinant host
organism, a said single chain specific binding pair member comprising a first
polypeptide chain component and a second polypeptide chain component and an amino
acid sequence encoded by a sequence provided by recombination between said sequences
at which site specific recombination occurs and specific for said complementary
specific binding pair member of interest, which single chain specific binding pair
comprises a polypeptide chain component which is as encoded by

nucleic acid encoding
a said polypeptide chain component of a specific binding pair member selected in
step (v) or is a derivative thereof by way of addition, deletion, substitution or
insertion of one or more amino acids or by linkage of another molecule.

15. A specific binding pair member according to claim 14 wherein the sequences at
which site-specific recombination occurs are loxP sequences and site-specific
recombination is catalysed by Cre-recombinase.

16. A specific binding pair member according to claim 14 wherein the first vectors
are phages or phagemids and the second vectors are plasmids, or the first vectors
are plasmids and the second vectors are phages or phagemids, and the intracellular
recombination takes place in a bacterial host which replicates plasmids
preferentially over phages or phagemids, or which replicates phages or phagemids
preferentially over plasmids.

17. A specific binding pair member according to claim 16 wherein said bacterial
host is a PolA strain of E. coli or of another gram-negative bacterium.

18. A specific binding pair member according to claim 17 which comprises an
antibody antigen-binding domain.

19. A specific binding pair member according to claim 14 which comprises a single
chain Fv immunoglobulin molecule.

US-PAT-NO: 6172197
DOCUMENT-IDENTIFIER: US 6172197 B1
TITLE: Methods for producing members of specific binding pairs
DATE-ISSUED: January 9, 2001
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McCafferty; John	Sawston	N/A	N/A	GBX
Pope; Anthony Richard	Cambridge	N/A	N/A	GBX
Johnson; Kevin Stuart	Cambridge	N/A	N/A	GBX
Hoogenboom; Henricus	Cambridge	N/A	N/A	GBX
Renerus Jacobus	Cambridge	N/A	N/A	GBX
Mattheus	Cambridge	N/A	N/A	GBX
Griffiths; Andrew David	Cambridge	N/A	N/A	GBX
Jackson; Ronald Henry	Cambridge	N/A	N/A	GBX
Holliger; Kaspar	Cambridge	N/A	N/A	GBX
Philipp	Buckingham	N/A	N/A	GBX
Marks; James David	Cambridge	N/A	N/A	GBX
Clackson; Timothy Piers	Cambridge	N/A	N/A	GBX
Chiswell; David John				
Winter; Gregory Paul				
Bonnert; Timothy Peter				

US-CL-CURRENT: 530/387.3,435/235.1 ,435/320.1 ,435/6 ,435/69.1 ,435/7.1 ,530/387.1 ,530/412 ,530/867 ,536/23.1 ,536/23.4 ,536/23.53

CLAIMS:

What is claimed is:
1. A library of filamentous bacteriophage particles displaying on their surface as a fusion with a gene III coat protein surface component a genetically diverse population of specific binding pair members in functional form comprising a binding domain for complementary binding specific binding pair members, said specific

binding pair members encoded by nucleic acid derived from a natural repertoire of
nucleic acids encoding said genetically diverse population of specific binding pair
members, the particles each containing a phagemid genome which is plasmid nucleic
acid containing a single stranded phage replication origin and a nucleotide sequence
encoding said fusion, and the particle having a coat partially derived from a helper
phage and partly from said fusion.

2. A library according to claim 1 wherein the specific binding pair members
comprise a binding domain of an immunoglobulin.

3. A library according to claim 2 wherein the specific binding pair members are
scFv molecules.

4. A library according to claim 2 wherein the specific binding pair members
comprise Fab molecules.

5. The library of claims 2, 3, or 4 wherein the natural repertoire of specific
binding pair members is encoded by nucleic acid derived from an animal unimmunized
against the complementary specific binding pair member.

6. The library of claims 2, 3, or 4 wherein the natural repertoire of specific
binding pair members is encoded by nucleic acid derived from an animal immunized
against the complementary specific binding pair member.

US-PAT-NO: 6140471
DOCUMENT-IDENTIFIER: US 6140471 A
TITLE: Methods for producing members of specific binding pairs
DATE-ISSUED: October 31, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Johnson; Kevin Stuart	Cambridge	N/A	N/A	GBX
Winter; Gregory Paul	Cambridge	N/A	N/A	GBX
Griffiths; Andrew David	Cambridge	N/A	N/A	GBX
Smith; Andrew John	Cambridge	N/A	N/A	GBX
Hammond	Canberra	N/A	N/A	AUX
Waterhouse; Peter Michael				

US-CL-CURRENT: 530/387.3

CLAIMS:

What is claimed is:

1. A specific binding pair memberwhich is a single chain specific binding pair member comprising a first polypeptide chain component and a second polypeptide chain component and which is specific for a complementary specific binding pair member of interest, produced by a method having the following steps:

(a) introducing into prokaryotic host cells

(i) first vectors comprising nucleic acid encoding a genetically diverse population of said first polypeptide chain component fused to a component of a secreted replicable genetic display package for display of said polypeptide chain components at the surface of replicable genetic display packages; and

(ii) second vectors comprising nucleic acid encoding a genetically diverse population of said second polypeptide chain components;

said first vectors being packaged in infectious replicable genetic display packages and their introduction into prokaryotic host cells being by infection into prokaryotic host cells harbouring said second vectors, or said second vectors being packaged in infectious replicable genetic display packages

and their introduction into prokaryotic host cells being by infection into host
cells harbouring said first vectors; and
(b) causing or allowing recombination between said first and second vectors within
said prokaryotic host cells, the recombination being promoted by inclusion in said
first and second vectors of sequences at which site-specific recombination occurs,
which sequences at which site-specific recombination occurs are derived from a loxP
sequence, resulting in recombinant vectors each of which comprises nucleic acid
encoding a said single chain specific binding pair member comprising a said first
polypeptide chain component and a said second polypeptide chain component and an
amino acid sequence encoded by a sequence provided by recombination between said
sequences at which site-specific recombination occurs, and capable of being packaged
into a replicable genetic display packages using said replicable genetic display
package component;
(c) expressing said single chain specific binding pair members, producing replicable
genetic display packages which display at their surface said single chain specific
binding pair members and which each comprise nucleic acid encoding a said single
chain specific binding pair member;
(d) selecting by binding with said complementary specific binding pair member of
interest one or more single chain specific binding pair members specific for said
complementary specific binding pair member of interest, each single chain specific
binding pair member thus selected being associated in its respective replicable
genetic display package with nucleic acid encoding that single chain specific
binding pair member;
(e) obtaining nucleic acid encoding a single chain specific binding pair member from
its replicable genetic display package displaying a specific binding pair member
selected in step (d);
(f) producing, by expression of encoding nucleic acid in a recombinant host
organism, a single chain specific binding pair member comprising a first polypeptide

chain component and a second polypeptide chain component and an amino acid sequence
encoded by a sequence provided by recombination between said sequences at which
site-specific recombination occurs and specific for said complementary specific
binding pair member of interest, which single chain specific binding pair comprises
a first polypeptide chain component which is as encoded by nucleic acid encoding a
said first polypeptide chain component of a specific binding pair member selected in
step (d) or is a derivative thereof by way of addition, deletion, substitution or
insertion of one or more amino acids or by linkage of another molecule, and a second
polypeptide chain component which is as encoded by nucleic acid encoding a said
second polypeptide chain component of a specific binding pair member selected in
step (d) or is a derivative thereof by way of addition, deletion, substitution or
insertion of one or more amino acids or by linkage of another molecule.

2. A specific binding pair member according to claim 1 comprising an antibody
antigen binding domain.

3. A specific binding pair member according to claim 2 which comprises a single
chain Fv molecule.

4. A specific binding pair member according to claim 1 wherein said replicable
genetic display packages are secreted bacteriophage.

5. A specific binding pair member according to claim 2 wherein said replicable
genetic display packages are secreted bacteriophage.

6. A specific binding pair member according to claim 3 wherein said replicable
genetic display packages are secreted bacteriophage.

7. A specific binding pair member according to claim 1 wherein the recombination
takes place in a bacterial host which replicates phages or phagemids preferentially
over plasmids.

8. A specific binding pair member according to claim 7 wherein said bacterial host
is a PolA strain of E. coli or of another gram-negative bacterium.

9. A specific binding pair member according to claim 2 wherein the recombination
takes place in a bacterial host which replicates phages or

phagemids preferentially
over plasmids.
10. A specific binding pair member according to claim 9 wherein said bacterial host
is a PolA strain of E. coli or of another gram-negative bacterium.
11. A specific binding pair member according to claim 3 wherein the recombination
takes place in a bacterial host which replicates phages or phagemids preferentially
over plasmids.
12. A specific binding pair member according to claim 11 wherein said bacterial
host is a PolA strain of E. coli or of another gram-negative bacterium.
13. A specific binding pair member according to claim 4 wherein the recombination
takes place in a bacterial host which replicates phages or phagemids preferentially
over plasmids.
14. A specific binding pair member according to claim 13 wherein said bacterial
host is a PolA strain of E. coli or of another gram-negative bacterium.
15. A specific binding pair member according to claim 5 wherein the recombination
takes place in a bacterial host which replicates phages or phagemids preferentially
over plasmids.
16. A specific binding pair member according to claim 15 wherein said bacterial
host is a PolA strain of E. coli or of another gram-negative bacterium.
17. A specific binding pair member according to claim 6 wherein the recombination
takes place in a bacterial host which replicates phages or phagemids preferentially
over plasmids.
18. A specific binding pair member according to claim 17 wherein said bacterial
host is a PolA strain of E. coli or of another gram-negative bacterium.

US-PAT-NO: 6017732
DOCUMENT-IDENTIFIER: US 6017732 A
TITLE: Bacteriophage library displaying immunoglobulin repertoires with a chemical
moiety covalently bound within the binding site: production and selection thereof
DATE-ISSUED: January 25, 2000
INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jespers; Laurent	Tervuren	N/A	N/A	BEX
Stephane Anne Therese	Cambridge	N/A	N/A	GBX
Winter; Gregory Paul	Seattle	WA	N/A	N/A
Bonnert; Timothy Peter	Bad	N/A	N/A	DEX
Simon; Thomas Martin	Krozingen-Hausen			

US-CL-CURRENT: 435/69.6,435/320.1 ,435/472 ,435/69.1 ,435/69.7 ,435/71.1 ,530/350
,530/387.1 ,530/387.3 ,530/402

CLAIMS:

We claim:
1. A diverse repertoire of first specific binding pair (sbp) members each having a
binding site for second sbp member and each being fused to a surface component of a
bacteriophage, wherein each first sbp member has a first polypeptide domain which
comprises a binding region of immunoglobulin heavy chain variable domain (VH) and a
second polypeptide domain which comprises a binding region of an immunoglobulin
light chain variable domain (VL), the first and in that each binding site comprises
a chemical moiety bound covalently at an amino acid residue within the binding site.
2. A method of providing a diverse repertoire of first specific binding pair (sbp)
members each of which has a binding site and is fused to a surface component of a
bacteriophage, each first sbp member having a first polypeptide domain which
comprises a binding region of an immunoglobulin heavy chain variable domain (VH) and
a second polypetide domain which comprises a binding of an

immunoglobulin light chain variable domain (VL), the first and second polypeptide domains forming the binding site, the method being characterized by a step of chemical modification of first sbp members in the repertoire to introduce a chemical moiety bound covalently to an amino acid residue in the binding site of each first sbp member.

3. A method according to claim 2 wherein provision of the repertoire of first sbp members before the step of chemical modification comprises expression from a population of nucleic acid molecules collectively encoding the repertoire.

4. A method according to claim 3 wherein provision of the population of nucleic acid molecules comprises a step of mutation of nucleic acid encoding first sbp member, or a polypeptide component part thereof, to introduce a codon encoding the amino acid residue.

5. A method according to claim 2 wherein the amino acid residue is selectively modified in each first sbp member.

6. A method according to claim 2 wherein the population of nucleic acid molecules is provided by joining gene fragments.

7. A method according to claim 2 wherein the chemical modification is performed in vitro.

8. A method according to claim 2 comprising, following said chemical modification, a step of selection of a first sbp member with a binding site able to bind a second sbp member of interest.

9. A method according to claim 8 wherein the selection is by binding with second sbp member of interest.

10. A method according to claim 8 wherein binding of the selected first sbp member to the second sbp member of interest is enhanced compared with binding of that first sbp member without said chemical moiety.

11. A method according to claim 8 wherein binding of the selected first sbp member to the second sbp member of interest is dependent on the presence of the chemical moiety bound covalently at said amino acid.

12. A method according to claim 8 wherein the first sbp members are expressed fused

to a surface component of a bacteriophage so that each bacteriophage in a population thereof thereby displays a first sbp member at its surface, each bacteriophage in the population containing a nucleic acid molecule which encodes the first sbp member displayed at its surface.

13. A method according to claim 12 wherein selection of a first sbp member with a binding site able to bind a second sbp member of interest is followed by recovery of a sequence of nucleotides from the bacteriophage which displays the selected first sbp member on its surface.

14. A method according to claim 13 wherein the sequence of nucleotides is used in the production of a first sbp member with a binding site able to bind that second sbp member of interest.

15. A method of providing a genetically diverse repertoire of first specific binding pair (sbp) members each of which has a binding site for complementary second sbp member and is fused to a surface component of a bacteriophage, each first sbp member having a first polypeptide domain which comprises a binding region of an immunoglobulin heavy chain variable domain (VH) and a second polypeptide domain which comprises a binding region of an immunoglobulin light chain variable domain (VL) the first and second polypeptide domains forming the binding site, the method comprising:

provision of a population of nucleic acid molecules collectively encoding a genetically diverse repertoire of first sbp members, the binding site of the encoded first sbp members each having an amino acid residue which is selectively modifiable to introduce a covalently bound chemical moiety into the binding site;

expression from the nucleic acid to provide a repertoire of first sbp members.

16. A method according to claim 15 wherein provision of the population of nucleic acid molecules comprises a step of mutation of nucleic acid encoding first sbp member, or a polypeptide component part thereof, to introduce a codon encoding the amino acid residue.

17. A method according to claim 15 wherein the population of nucleic acid molecules
is provided by joining gene fragments.
18. A method according to claim 15 comprising chemical modification of first sbp
members in the repertoire thereof at said amino acid residue to introduce a
covalently bound chemical moiety into the binding site.
19. A method according to claim 18 comprising, following said chemical
modification, a step of selection of first sbp member with a binding site able to
bind a second sbp member of interest.
20. A method according to claim 19 wherein the selection is by binding with second
sbp member of interest.
21. A method according to claim 19 wherein binding of the selected first sbp member
to the second sbp member of interest is enhanced compared with binding of that first
sbp member without said chemical moiety.
22. A method according to claim 19 wherein binding of the selected first sbp member
to the second sbp member of interest is dependent on the presence of the chemical
moiety bound covalently at the amino acid.
23. A method according to claim 19 wherein the first sbp members are expressed
fused to a surface component of a bacteriophage so that each bacteriophage in a
population thereof thereby displays a first sbp member at its surface, each
bacteriophage in the population containing a nucleic acid molecule which encodes the
first sbp member displayed at it surface.
24. A method according to claim 23 wherein selection of a first sbp member with a
binding site able to bind a second sbp member of interest is followed by recovery of
a sequence of nucleotides from the bacteriophage which displays the selected first
sbp member on its surface.
25. A method according to claim 24 wherein the sequence of nucleotides is used in
the production of a first sbp member with a binding site able to bind that second
sbp member of interest.